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NOTICE OF ALLOWANCE AND FEE(S) DUE

2292

7590

05/28/2009

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER

MYERS, CARLA J

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 05/28/2009

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------------|---------------------|------------------|
| 10/695,744 | 10/30/2003 | Patrizia Paterlini-Brechot | 2121-0178P | 7652 |
| TITLE OF INVENTION: PRENATAL DIAGNOSIS METHOD ON ISOLATED FOETAL CELL OF MATERNAL BLOOD | | | | |

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE |
|----------------|--------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | NO | \$1510 | \$300 | \$0 | \$1810 | 08/28/2009 |

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. **PROSECUTION ON THE MERITS IS CLOSED.** THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN **THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE** OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. **THIS STATUTORY PERIOD CANNOT BE EXTENDED.** SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
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 or Fax **(571)-273-2885**

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

2292 7590 05/28/2009

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

| |
|--------------------|
| (Depositor's name) |
| (Signature) |
| (Date) |

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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10/695,744

10/30/2003

Patrizia Paterlini-Brechot

2121-0178P

7652

TITLE OF INVENTION: PRENATAL DIAGNOSIS METHOD ON ISOLATED FOETAL CELL OF MATERNAL BLOOD

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE |
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| EXAMINER | ART UNIT | CLASS-SUBCLASS |
|----------------|----------|----------------|
| MYERS, CARLA J | 1634 | 435-006000 |

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB-122) attached.
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB-47; Rev 03-02 or more recent) attached. Use of a **Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 _____
 (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 _____
 3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.111. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee
☐ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____
 Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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| BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747 | | | MYERS, CARLA J | |
| | | | ART UNIT | PAPER NUMBER |

1634

DATE MAILED: 05/28/2009

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability

Application No.

10/695,744

Examiner

Carla Myers

Applicant(s)

PATERLINI-BRECHOT, PATRIZIA

Art Unit

1634

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 4/15/09.
2. ☒ The allowed claim(s) is/are 1,4,5,9,11-18,20-22,25,30 and 31.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some* c) ☐ None of the:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Linda Parker on May 20, 2009.

The application has been amended as follows:

In the specification, at page 1, line 1, the following sentence has been inserted:
-- This application is a continuation of PCT International Application No. PCT/FR02/01505, filed April 30, 2002.--

The claims have been amended as follows:

In claim 1, line 3, after "a) diluting a sample of maternal blood", the phrase --collected from a pregnant woman between the 5th and 15th week of pregnancy-- has been inserted.

In claim 1, line 5, "collected from a pregnant woman between the 5th and 15th week of pregnancy" has been deleted.

In claim 9, line 1, "identification of" has been deleted and --identifying-- has been inserted therefor.

In claim 13, line 1, "identification of" has been deleted and --identifying-- has been inserted therefor.

In claim 18, line 3, "preamplified DNA preparation" has been deleted and --preparation of preamplified DNA-- has been inserted therefor.

The claims have been renumbered so that claims 14-16 and 18 depend from a previous claim, rather than a subsequent claim. The final claim numbers are: original claim 1 is final claim 1; claim 4 is final claim 2; claim 5 is final claim 3; claim 9 is final claim 4; claim 11 is final claim 5; claim 12 is final claim 6; claim 13 is final claim 7; claim 14 is final claim 15; claim 15 is final claim 16; claim 16 is final claim 17; claim 17 is final claim 8; claim 18 is final claim 18; claim 20 is final claim 9; claim 21 is final claim 10; claim 22 is final claim 11; claim 25 is final claim 12; claim 30 is final claim 13; claim 31 is final claim 14.

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance:

The closest prior art of Kalionis (WO 99/15892) teaches "a method for easily enriching and identifying trophoblast cells in maternal peripheral blood in the presence of a population of blood cell types. The enrichment, identification and analysis of trophoblast cells in peripheral blood provides a means by which non- invasive prenatal diagnosis can be carried out. This method is therefore of particular value in prenatal testing to obtain genetic and/or biochemical information about the fetus" (page 3). The method of Kalionis (pages 5-7) comprises the steps of: a) diluting a sample of maternal blood in a solution comprising a reagent for lysing red blood cells; b) filtering the diluted sample of maternal blood through a filter according to size, in order to separate fetal

cells from maternal blood cells; c) analyzing the cells retained on the filter by immunostaining for trophoblast- specific markers, in order to confirm the identify of the cells as being of fetal origin (see also page 8); d) analyzing individual cells by in situ hybridization and immunostaining to demonstrate that the cells are fetal cells (see also pages 10 and 18); and e) analyzing the individual fetal cells to detect a genetic anomaly or to determine the sex of the fetal cells (see also pages 9-10 and page 21).

Kalionis does not teach collecting the individual fetal cells retained on the filter by microdissection, wherein the microdissection uses a laser to recover single collected cells in a tube, and analyzing the isolated fetal cells by lysing the cells, pre-amplifying the cells and using the preamplification product to demonstrate the fetal origin of the isolated cells and to carry out prenatal diagnosis. Further, while Kalionis (page 4) teaches filtering the maternal blood through a filter having a pore size of 10 μm , Kalionis does not teach or suggest filtering the maternal blood sample through a filter with a pore size of 8 μm and a pore density in the range of 5×10^4 to 5×10^5 pores/ cm^2 wherein a filtration pressure of 0.05 to 0.8 bars is applied to the filter. Moreover, Kalionis only teaches application of the method to the analysis of maternal blood samples obtained at weeks 30-37 of pregnancy (page 21). It was well known in the art at the time the invention was made that fetal cells are present at relatively low numbers in maternal blood and that the number of fetal cells in maternal blood increases with the stage of pregnancy. For instance, Kalionis teaches that at 30 weeks of pregnancy, there were 37 fetal trophoblast cells/20ml in a maternal blood sample from a woman who had been diagnosed with PIH; at 32 weeks of pregnancy, there were 59 trophoblast cells/20 ml in

a maternal blood sample from a woman who had been diagnosed with PIH; and at 35 weeks of pregnancy, there were 82 trophoblast cells in a maternal blood sample from a woman who had been diagnosed with PIH. In samples from woman without PIH, there were 5, 7 and 8 trophoblasts/20 ml of maternal blood samples obtained at weeks 32, 33 and 37 of pregnancy. Kalonis does not teach or suggest or provide the guidance to enable the claimed method in which the maternal blood sample to be analyzed for prenatal diagnosis of fetal cells is obtained from a pregnant woman between the 5th and 15th week of pregnancy, particularly wherein the maternal blood sample obtained between the 5th and 15th week of pregnancy is filtered through a filter with a pore size of 8 μ m and a pore density in the range of 5×10^4 to 5×10^5 pores/cm², under an applied filtration pressure of 0.05 to 0.8 bars, in order to retain epithelial cells on the filter, and wherein the epithelial cells retained on the filter are subsequently analyzed for an immunological or cytological marker to permit the collection of a single cell which is identified as a fetal trophoblastic or syncytiotrophoblastic cell based on the presence of the immunological or cytological marker.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Carla Myers/

Primary Examiner, Art Unit 1634